ds

Set	Items	Description
S1	259	AAV AND (AIRWAY OR INTRANASAL?)
S2	101	RD (unique items)
S3	11	S2 AND (AAV5 OR AAV-5 OR AAV(W)5)
S4	66	S2 NOT PY>2000
S5	10	S4 AND ALVEOL?

Amy
Dialog (file: medicine)
6/26/03

5/3,AB/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10138025 BIOSIS NO.: 199698592943
Alveolar **stem cell transduction by an adeno-associated viral vector.**
AUTHOR: Zeitlin P L(a); Chu S; Conrad C; McVeigh U; Ferguson K; Flotte T R; Guggino W B
AUTHOR ADDRESS: (a)Park 316, Dep. Pediatrics, Johns Hopkins Hosp., 600 North Wolfe St., Baltimore, MD 21287**USA
JOURNAL: Gene Therapy 2 (9):p623-631 1995
ISSN: 0969-7128
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: In inherited disorders such as surfactant protein deficiency or cystic fibrosis (CF), where lung damage developed progressively after birth, gene replacement is best accomplished in the neonatal period. We use the adeno-associated virus (**AAV**) as a vector for gene transfer in the newborn rabbit lung where stem cells are activated for lung growth and differentiation. **AAV** -mediated gene transfer as assayed by lacZ gene expression occurred preferentially in **alveoli** in the **alveolar** epithelial progenitor cell, the type II cell, and in the large **airway** tracheobronchial basal and ciliated cells. Cell proliferation was confirmed by 5-bromo-deoxyuridine (BRDU) labeling in regions undergoing **alveolarization** and **airway** branch points. Regions of cell proliferation coincided with areas of significant lacZ expression. Thus, dividing and differentiating cells can be targeted by AAVlacZ delivery to newborn lung.

1995

5/3,AB/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12473599 BIOSIS NO.: 200000227101
Adeno-associated virus type 5 (AAV5) but not AAV2 binds to the apical surfaces of airway epithelia and facilitates gene transfer.
AUTHOR: Zabner Joseph(a); Seiler Michael; Walters Robert; Kotin Robert M; Fulgeras Wendy; Davidson Beverly L; Chiorini John A
AUTHOR ADDRESS: (a)University of Iowa College of Medicine, 500 EMRB, Iowa City, IA, 52242**USA
JOURNAL: Journal of Virology 74 (8):p3852-3858 April, 2000
ISSN: 0022-538X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: In the genetic disease cystic fibrosis, recombinant adeno-associated virus type 2 (AAV2) is being investigated as a vector to transfer CFTR cDNA to **airway** epithelia. However, earlier work has shown that the apical surface of human **airway** epithelia is resistant to infection by AAV2, presumably as a result of a lack of heparan sulfate proteoglycans on the apical surface. This inefficiency can be overcome by increasing the amount of vector or by increasing the incubation time. However, these interventions are not very practical for translation into a therapeutic **airway** -directed vector. Therefore, we examined the efficiency of other **AAV** serotypes at infecting human **airway** epithelia. When applied at low multiplicity of infection to the apical surface of differentiated **airway** epithelia we found that a recombinant AAV5 bound and mediated gene transfer 50-fold more efficiently than AAV2. Furthermore, in contrast to AAV2, AAV5-mediated gene transfer was not inhibited by soluble heparin. Recombinant AAV5 was also more efficient than AAV2 in transferring beta-galactosidase cDNA to murine **airway** and **alveolar** epithelia in vivo. These data suggest that AAV5-derived vectors bind and mediate gene transfer to human and murine **airway** epithelia, and the tropism of AAV5 may be useful to target cells that are not permissive for AAV2.

2000

5/3,AB/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12357452 BIOSIS NO.: 200000110954
Repeat transduction in the mouse lung by using adeno-associated virus vectors with different serotypes.
AUTHOR: Halbert Christine L; Rutledge Elizabeth A; Allen James M; Russell David W; Miller A Dusty(a)
AUTHOR ADDRESS: (a)Fred Hutchinson Cancer Research Center, 1100 Fairview Ave. North, Room C2-023, Seattle, WA, 98109-1024**USA
JOURNAL: Journal of Virology 74 (3):p1524-1532 Feb., 2000
ISSN: 0022-538X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Vectors derived from adeno-associated virus type 2 (AAV2) promote gene transfer and expression in the lung; however, we have found that while gene expression can persist for at least 8 months in mice, it was reduced dramatically in rabbits over a period of 2 months. The efficiency and persistence of AAV2-mediated gene expression in the human lung have yet to be determined, but it seems likely that readministration will be necessary over the lifetime of an individual. Unfortunately, we have

found that transduction by a second administration of an AAV2 vector is blocked, presumably due to neutralizing antibodies generated in response to the primary vector exposure. Here, we have explored the use of AAV2 vectors pseudotyped with capsid proteins from **AAV** serotypes 2, 3, and 6 for readministration in the mouse lung. We found that an AAV6 vector transduced **airway** epithelial and **alveolar** cells in the lung at rates that were at least as high as those of AAV2 pseudotype vectors, while transduction rates mediated by AAV3 were much lower. AAV6 pseudotype vector transduction was unaffected by prior administration of an AAV2 or AAV3 vector, and transduction by an AAV2 pseudotype vector was unaffected by prior AAV6 vector administration, showing that cross-reactive neutralizing antibodies against AAV2 and AAV6 are not generated in mice. Interestingly, while prior administration of an AAV2 vector completely blocked transduction by a second AAV2 pseudotype vector, prior administration of an AAV6 vector only partially inhibited transduction by a second administration of an AAV6 pseudotype vector. Analysis of sera obtained from mice and humans showed that AAV6 is less immunogenic than AAV2, which helps explain this finding. These results support the development of AAV6 vectors for lung gene therapy both alone and in combination with AAV2 vectors.

2000

5/3,AB/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12213965 BIOSIS NO.: 199900508814
Successful readministration of adeno-associated virus vectors to the mouse lung requires transient immunosuppression during the initial exposure.
AUTHOR: Halbert Christine L; Standaert Thomas A; Wilson Christopher B; Miller A Dusty(a)
AUTHOR ADDRESS: (a)Fred Hutchinson Cancer Res. Cent., 1100 Fairview Ave. North, Room C2-023, Seattle, WA 98109-1024**USA
JOURNAL: Journal of Virology 72 (12):p9795-9805 Dec., 1998
ISSN: 0022-538X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The **airway** is an important target for gene transfer to treat cystic fibrosis and other diseases that affect the lung. We previously found that marker gene expression did not persist in the bronchial epithelium following adeno-associated virus (**AAV**) vector administration to the rabbit lung. In an attempt to promote continued expression, we tested repeat vector administration, but no additional transduction was observed, and the block to transduction correlated with the appearance of neutralizing antibodies to the viral capsid. Here we show that mice exhibit a similar response but that treatment with anti-CD40 ligand antibody (MRI) and a soluble CTLA4-immunoglobulin fusion protein (CTLA4Ig) at the time of primary **AAV** vector exposure allowed successful repeat transduction and prevented production of neutralizing antibodies. We also tested the possibility that an immune response caused the loss of marker-positive cells in the epithelial population in rabbits by evaluating **AAV** vector expression in immunocompetent and immunodeficient mice. In contrast to results in rabbits, marker protein expression persisted in the lung in both groups of mice. **AAV** vector transduction occurred in **alveolar** cells, **airway** epithelial cells, and smooth muscle cells, and vector expression persisted for at least 8 months. Although data on persistence of **AAV** vector expression in the human lung are not available, it is likely that repeat transduction will be necessary either due to loss of expression or to the need for repeat administration to deliver effective amounts of **AAV** vectors. Results presented here indicate that transient immunosuppression will allow such repeat vector treatment of the lung.

1998

5/3,AB/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10138025 BIOSIS NO.: 199698592943
Alveolar **stem cell transduction by an adeno-associated viral vector.**
AUTHOR: Zeitlin P L(a); Chu S; Conrad C; McVeigh U; Ferguson K; Flotte T R; Guggino W B
AUTHOR ADDRESS: (a)Park 316, Dep. Pediatrics, Johns Hopkins Hosp., 600 North Wolfe St., Baltimore, MD 21287**USA
JOURNAL: Gene Therapy 2 (9):p623-631 1995
ISSN: 0969-7128
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: In inherited disorders such as surfactant protein deficiency or cystic fibrosis (CF), where lung damage developed progressively after birth, gene replacement is best accomplished in the neonatal period. We use the adeno-associated virus (**AAV**) as a vector for gene transfer in the newborn rabbit lung where stem cells are activated for lung growth and differentiation. **AAV** -mediated gene transfer as assayed by lacZ gene expression occurred preferentially in **alveoli** in the **alveolar** epithelial progenitor cell, the type II cell, and in the large **airway** tracheobronchial basal and ciliated cells. Cell proliferation was confirmed by 5-bromo-deoxyuridine (BRDU) labeling in regions undergoing **alveolarization** and **airway** branch points. Regions of cell proliferation coincided with areas of significant lacZ expression. Thus, dividing and differentiating cells can be targeted by AAVlacZ delivery to newborn lung.

1995

5/3,AB/5 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

09305119 Genuine Article#: 389EF Number of References: 28
Title: Perfluorochemical liquid enhances adeno-associated virus-mediated transgene expression in lungs (ABSTRACT AVAILABLE)
Author(s): Weiss DJ (REPRINT) ; Bonneau L; Allen JM; Miller AD; Halbert CL
Corporate Source: Fred Hutchinson Canc Res Ctr,Div Pulm & Crit Care Med,1100 Fairview Ave N/Seattle//WA/98109 (REPRINT); Fred Hutchinson Canc Res Ctr,Div Pulm & Crit Care Med,Seattle//WA/98109; Fred Hutchinson Canc Res Ctr,Div Human Biol,Seattle//WA/98109
Journal: MOLECULAR THERAPY, 2000, V2, N6 (DEC), P624-630
ISSN: 1525-0016 Publication date: 20001200
Publisher: ACADEMIC PRESS INC, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495 USA
Language: English Document Type: ARTICLE
Abstract: Use of adeno-associated virus (**AAV**) vectors for lung gene therapy is limited, in part, by low levels of **AAV** -mediated transgene expression in lungs. Generally, less than 1% of total **airway** and **alveolar** epithelial cells express transgene activity following vector administration. A means of improving **AAV** vector delivery could potentially enhance **AAV** -mediated gene expression in lungs. We have previously demonstrated that use of perfluorochemical (PFC) liquids improved overall levels of adenovirus vector-mediated gene expression as well as distribution of expression in lungs of spontaneously breathing rodents. To evaluate whether use of PFC liquids might similarly enhance **AAV** -mediated expression, spontaneously breathing rodents received intratracheal instillation of the **AAV** vectors CWRAP and ARAP4 (2-5 x 10(8) FFU/animal) with or without 10 cc/kg body wt PFC

liquid (FC-75, ACROS). Animals were sacrificed 4 weeks later and lungs assessed for overall and in situ alkaline phosphatase (AP) expression. Animals receiving vector alone exhibited scattered sparse in situ activity, predominantly in **alveolar** epithelium. In contrast, animals receiving vector with FC-75 exhibited increased and more widespread AP expression as well as up to a 26-fold increase in AP activity. These results demonstrate that use of the PFC liquid FC-75 improves overall and in situ **AAV** -mediated gene expression in rodent lungs.

5/3,AB/6 (Item 1 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)

01760433 SUPPLIER NUMBER: 20313191 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Cystic fibrosis. (review article)
Rosenstein, Beryl J.; Zeitlin, Pamela L.
The Lancet, v351, n9098, p277(6)
Jan 24,
1998
PUBLICATION FORMAT: Magazine/Journal; Refereed ISSN: 0099-5355
LANGUAGE: English RECORD TYPE: Fulltext; Abstract TARGET AUDIENCE: Professional
WORD COUNT: 5868 LINE COUNT: 00485

ABSTRACT: Cystic fibrosis (CF) is a genetic disease characterized by persistent respiratory infections, **airway** obstruction, intestinal, metabolic and pancreatic diseases. Many neonatal screening programs routinely test for this defect, and patients with symptoms may be diagnosed by testing of blood and sweat, and genetic evaluation. Therapy is focused on antibiotic control of infection, improving lung function, and ensuring adequate nutrition. Lung transplantation can be effective in end-stage disease. New therapies are being investigated. In the US, patients survive about 30 years with CF.

5/3,AB/7 (Item 2 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)

01619731 SUPPLIER NUMBER: 18306605 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Cystic fibrosis in adults: from researcher to practitioner.
Marelich, Gregory P.; Cross, Carroll E.
The Western Journal of Medicine, v164, n4, p321(14)
April,
1996
PUBLICATION FORMAT: Magazine/Journal ISSN: 0093-0415 LANGUAGE: English
RECORD TYPE: Fulltext; Abstract TARGET AUDIENCE: Professional
WORD COUNT: 13175 LINE COUNT: 01133

AUTHOR ABSTRACT: The Cystic Fibrosis Foundation currently tracks about 20,000 Americans with cystic fibrosis, an autosomal recessive genetic disease that leads to multisystem complications. With the institution of better therapeutic regimens over the past 2 decades, more patients with this disease are surviving to adulthood. Within the past decade, both clinical and basic science research in the field of cystic fibrosis has progressed at a rapid rate. The intent of this review is to introduce readers to the molecular, cellular, and systemic disorders of this disease. We discuss treatment strategies involving antibiotics, nutrition, immune-response mediators, chest physiotherapy, and sputum-active agents with respect to the **airway** dysfunction of cystic fibrosis. Other common complications, recent developments, transplantation, and gene therapy are also reviewed.

5/3,AB/8 (Item 3 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)

01426625 SUPPLIER NUMBER: 14376933 (USE FORMAT 7 OR 9 FOR FULL TEXT)

The basic science of gene therapy.

Mulligan, Richard C.

Science, v260, n5110, p926(7)
May 14,
1993
PUBLICATION FORMAT: Magazine/Journal ISSN: 0036-8075 LANGUAGE: English
RECORD TYPE: Fulltext; Abstract TARGET AUDIENCE: Academic
WORD COUNT: 7618 LINE COUNT: 00623

AUTHOR ABSTRACT: The development over the past decade of methods for delivering genes to mammalian cells has stimulated great interest in the possibility of treating human disease by gene-based therapies. However, despite substantial progress, a number of key technical issues need to be resolved before gene therapy can be safely and effectively applied in the clinic. Future technological developments, particularly in the areas of gene delivery and cell transplantation, will be critical for the successful practice of gene therapy.

5/3,AB/9 (Item 1 from file: 266)

DIALOG(R)File 266:FEDRIP

00345110
IDENTIFYING NO.: 5U01HL66947-03 0003 AGENCY CODE: CRISP
GENE THERAPY FOR CYSTIC FIBROSIS USING AAV **VECTORS**

PRINCIPAL INVESTIGATOR: MILLER, ARTHUR D
ADDRESS: UNIVERSITY OF WASHINGTON 1705 NE PACIFIC K-253B SEATTLE, WA 98195
PERFORMING ORG.: UNIVERSITY OF WASHINGTON, SEATTLE, WASHINGTON
SPONSORING ORG.: NATIONAL HEART, LUNG, AND BLOOD INSTITUTE
DATES: 2009/28/00 TO 2008/31/05 FY : 2002

SUMMARY: Gene Therapy for Cystic Fibrosis using **AAV** Vectors. Cystic fibrosis (CF) affects 1 in 3,200 births and leads to debilitating lung disease and premature death at a median age of 32 years. Gene therapy may provide a cure for this disease by replacement of the defective protein, the cystic fibrosis transmembrane regulator (CFTR). The long-range objective of this application is the development of lung-targeted gene therapy for treatment of CF using viral vectors derived from a non-pathogenic human parvovirus, adeno-associated virus (**AAV**). **AAV** vectors have been shown to promote gene transfer and long-term expression in several animal models, in particular, **AAV** vectors can transduce **airway** and **alveolar** epithelial cells in the lungs of mice at rates of greater than or equal to 5% and lasting for over 8 months. However, clinical trials involving **AAV** vector-mediated transfer of the CFTR gene to humans have yet to show useful levels of CFTR expression or clinical efficacy. This lack of expression is likely due to the difficulty of making **AAV** vectors that express CFTR because of the large size of the CFTR cDNA, and the difficulty of measuring small changes in CF disease severity that might result from gene therapy. To circumvent these difficulties and to provide a more direct test of the utility of **AAV** vectors in humans, the specific aims of this proposal include clinical trials in healthy subjects and CF patients which will address the safety, efficacy, and immune responses to nasal and bronchial administration of **AAV** vectors that encode an easily detected histochemical marker gene, human placental alkaline phosphatase (hpAp). We have found that vectors derived from **AAV** serotype 6 show improved transduction rates in mouse **airway** compared to commonly used **AAV** serotype 2 vectors, although more extensive safety data in humans is available for AAV2. Here we propose to compare expression of hpAP extensive safety data in humans is available for AAV2. Here we propose to compare expression of hpAP delivered by both AAV2 and AAV6 in healthy subjects. The vector serotype with the better safety and gene expression profile will be tested subsequently in patients with CF. Another specific aim will address the development of effective **AAV** vectors for transfer

and efficient expression of the CFTR cDNA. These approaches are designed to most efficiently test and develop **AAV** vectors for treatment of CF.

5/3,AB/10 (Item 1 from file: 442)

00087881

Gene Delivery Systems in Surgery (ARTICLE)

LYERLY, H. KIM
Archives of Surgery
Nov, 1993; Original Article: p1197
LINE COUNT: 00737

Increased understanding of the genetic basis of human disease has ledto a number of potential gene-based therapies for various medical andsurgical disorders. The development of efficient methods for delivering genes to mammalian cells in vitro has increased the potential clinical utility of gene-based therapies; however, a major focus of research has been more efficient delivery to appropriate target cells, in vivo as well as in vitro, to establish gene therapy as an effective clinical modality for common disorders. Despite substantial progress, a number of critical technical issues to enhance and optimize not only gene transfer but also gene expression must be resolved. These future technological developments will be essential for the widespread clinical implementation of gene-based therapy. (Arch Surg. 1993;128:1197-1206)
?

3/3,AB/11 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

132009654 CA: 132(2)9654t PATENT
Aav5 vector with therapeutic applications for transduction of airway epithelium
INVENTOR(AUTHOR): Chiorini, John A.; Kotin, Robert M.
LOCATION: USA
ASSIGNEE: United States of America, Department of Health and Human Services
PATENT: PCT International ; WO 9961601 A2 DATE: 19991202
APPLICATION: WO 99US11958 (19990528) *US 87029 (19980528)
PAGES: 91 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C12N-015/00A
DESIGNATED COUNTRIES: AE; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; CA; CH; CN; CU; CZ; DE; DK; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MD; MG; MK; MN; MW; MX; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; UA; UG; US; UZ; VN; YU; ZA; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM
DESIGNATED REGIONAL: GH; GM; KE; LS; MW; SD; SL; SZ; UG; ZW; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; GW; ML; MR; NE; SN; TD; TG
?

Set	Items	Description
S1	154	AAV5
S2	49	RD (unique items)
S3	18	S2 NOT PY>2000
S4	1	S3 AND ALVEOLAR
S5	3	S3 AND CEREBELLA?
S6	1	S3 AND EPENDYMA?
S7	0	AAV-5
S8	130	AAV(W)5
S9	74	S8 NOT PY>2000
S10	0	S9 AND ALVEOLA?
S11	0	S9 AND EPENDYMA?
S12	0	S9 AND CEREBELLA?

?

Dialog
file: medicine

Amy
6/26/03

4/3,AB/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12473599 BIOSIS NO.: 200000227101
Adeno-associated virus type 5 (AAV5) but not AAV2 binds to the apical surfaces of airway epithelia and facilitates gene transfer.
AUTHOR: Zabner Joseph(a); Seiler Michael; Walters Robert; Kotin Robert M; Fulgeras Wendy; Davidson Beverly L; Chiorini John A
AUTHOR ADDRESS: (a)University of Iowa College of Medicine, 500 EMRB, Iowa City, IA, 52242**USA
JOURNAL: Journal of Virology 74 (8):p3852-3858 April, 2000
ISSN: 0022-538X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: In the genetic disease cystic fibrosis, recombinant adeno-associated virus type 2 (AAV2) is being investigated as a vector to transfer CFTR cDNA to airway epithelia. However, earlier work has shown that the apical surface of human airway epithelia is resistant to infection by AAV2, presumably as a result of a lack of heparan sulfate proteoglycans on the apical surface. This inefficiency can be overcome by increasing the amount of vector or by increasing the incubation time. However, these interventions are not very practical for translation into a therapeutic airway-directed vector. Therefore, we examined the efficiency of other AAV serotypes at infecting human airway epithelia. When applied at low multiplicity of infection to the apical surface of differentiated airway epithelia we found that a recombinant **AAV5** bound and mediated gene transfer 50-fold more efficiently than AAV2. Furthermore, in contrast to AAV2, **AAV5** -mediated gene transfer was not inhibited by soluble heparin. Recombinant **AAV5** was also more efficient than AAV2 in transferring beta-galactosidase cDNA to murine airway and **alveolar** epithelia in vivo. These data suggest that **AAV5** -derived vectors bind and mediate gene transfer to human and murine airway epithelia, and the tropism of **AAV5** may be useful to target cells that are not permissive for AAV2.

2000

5/3,AB/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12680524 BIOSIS NO.: 200000434026
Transduction of murine cerebellar **neurons with recombinant FIV and** AAV5 **vectors.**
AUTHOR: Alisky Joseph M; Hughes Stephanie M; Sauter Sybille L; Jolly Douglas; Dubensky Thomas W Jr; Staber Patrick D; Chiorini John A; Davidson Beverly L(a)
AUTHOR ADDRESS: (a)Program in Gene Therapy, Department of Internal Medicine, University of Iowa College of Medicine, Iowa City, IA, 52242** USA
JOURNAL: Neuroreport 11 (12):p2669-2673 21 August, 2000
MEDIUM: print
ISSN: 0959-4965
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Our data demonstrate that vectors derived from recombinant feline immunodeficiency virus (rFIV) and adeno-associated virus type 5 (rAAV5) transduce **cerebellar** cells following direct injection into the **cerebellar** lobules of mice. Both recombinant viruses mediated gene transfer predominantly to neurons, with up to 2500 and 1500 Purkinje cells transduced for rAAV5 or rFIV-based vectors, respectively. The vectors also transduced stellate, basket and Golgi neurons, with occasional transduction of granule cells and deep **cerebellar** nuclei. rAAV5 also spread outside the cerebellum to the inferior colliculus and ventricular epithelium, while rFIV demonstrated the ability to undergo retrograde transport to the physically close lateral vestibular nuclei. Thus, **AAV5** and FIV-based vectors show promise for targeting neurons affected in the hereditary spinocerebellar ataxias. These vectors could be important tools for unraveling the pathophysiology of these disorders, or in testing factors which may promote neuronal survival.

2000

5/3,AB/2 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

09070868 Genuine Article#: 363JX Number of References: 2
Title: Transduction of murine cerebellar **neurons with recombinant FIV and** AAV5 **vectors (vol 11, pg 2669, 2000)**
Author(s): Alisky JM
Journal: NEUROREPORT, 2000, V11, N14 (SEP 28), PCOV3-COV3
ISSN: 0959-4965 Publication date: 20000928
Publisher: LIPPINCOTT WILLIAMS & WILKINS, 530 WALNUT ST, PHILADELPHIA, PA 19106-3621
Language: English Document Type: CORRECTION, ADDITION

5/3,AB/3 (Item 1 from file: 135)
DIALOG(R)File 135:NewsRx Weekly Reports

0000041098 (USE FORMAT 7 OR 9 FOR FULLTEXT)
Neurons Successfully Transduced with Recombinant FIV and AAV5 **Vectors**
Gene Therapy Weekly, November 2, 2000, p.10

DOCUMENT TYPE: Expanded Reporting LANGUAGE: English
RECORD TYPE: FULLTEXT
WORD COUNT: 317
?

6/3,AB/1 (Item 1 from file: 266)
DIALOG(R)File 266:FEDRIP

00336104
IDENTIFYING NO.: 1F32HD08692-01 AGENCY CODE: CRISP
MPS VII TREATMENT USING AAV4 AND AAV5 **VECTORS**
PRINCIPAL INVESTIGATOR: HETH, JASON A
ADDRESS: JASON-HETH@UIOWA.EDU UNIV OF IOWA HOSP & CLINICS 200 HAWKINS DRIVE IOWA CITY, IA 52242
PERFORMING ORG.: UNIVERSITY OF IOWA, IOWA CITY, IOWA
SPONSORING ORG.: NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT
DATES: 2001/10/01 FY : 2000
SUMMARY: Lysosomal storage diseases(LSDs) result from deficiencies of lysosomal enzymes leading to accumulation of precursor products. The stored material eventually leads to diffuse tissue disease and premature death. Mucopolysaccharidosis VII(MPS VII) is a representative LSD characterized by absent or severely decreased levels of B-glucuronidase, with both CNS and systemic involvement. Gene transfer strategies are being investigated as a therapy to provide for a long-lasting, endogenous source of beta-glucuronidase. Preliminary data obtained with recombinant adeno-associated viruses types 4 and 5(AAV4 and **AAV5**) reporter viruses suggest that AAV4 or **AAV5** could efficiently mediate beta-glucuronidase gene transfer to brain. As such, we propose experiments to better understand these novel vectors and to investigate their ability to correct LSD in brain. These experiments are to answer the following questions: SPECIFIC AIM 1: Can **AAV5** -beta-glucuronidase correct lysosomal storage diseases in the CNS of the MPSVII mouse? SPECIFIC AIM 2: Is there a polarity to AAV4-mediated **ependymal** cell transduction? SPECIFIC AIM 3: Can the extent of gene transfer with AAV4 and **AAV5** be increased by delivery through minipumps? SPECIFIC AIM 4: Can AAV4 and **AAV5** transduce cells in human brain tissue?
?